

impact of tracheal intubation in this setting. We can, however, infer from these data that physiologic and anatomical difficulty are not mutually exclusive. First-pass success is a surrogate for overall ease of performing the tracheal intubation procedure, and a high or low rate of success in this measure informs the likelihood of encountering delays in securing the airway and prolonged apnea times that would then result in physiologic deterioration. In the event of this deterioration, cessation of tracheal intubation attempts may be prompted in exchange for bag-mask ventilation or cardiovascular stabilization with vasopressor administration. Thus, first-pass success may indeed be a meaningful indicator for physiologically difficult airways. Delving into our data, this may be the underlying reason for rapid sequence induction being associated with an improved first-pass success rate, as abandoning tracheal intubation attempts in exchange for optimizing physiology is less likely. This may dovetail into the discussion of early *versus* late tracheal intubation attempts, with early intubation potentially associated with greater physiologic stability than late tracheal intubation.<sup>4</sup>

Ultimately, however, we acknowledge that further studies incorporating patient-level physiologic variables and other outcome measures may be required to investigate particular patient factors to inform airway managers in their approaches to mitigate risk. Although all studies have limitations, we began the pandemic with little or no information, and multicenter collaborative studies such as intubateCOVID have needed to move quickly to provide evidence to inform clinicians and improve the quality of patient care.

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### Competing Interests

The authors declare no competing interests.

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## Individualized Fluid and Vasopressor Therapy: Comment

To the Editor:

We read with great interest the randomized controlled trial published recently by Joosten *et al.* in *ANESTHESIOLOGY*.<sup>1</sup> This study assessed the ability of a closed-loop system for the titration of a norepinephrine infusion combined with a fluid-management decision support system to decrease the percentage of intraoperative time at risk for tissue hypoperfusion when compared with a “traditional” manually controlled goal-directed hemodynamic optimization. The authors reported that patients in the computer-assisted group had significantly less total intraoperative time with hypotension (primary outcome), less oscillation in mean arterial pressure (MAP) during surgery, and a higher mean cardiac index at the end of the procedure—while also receiving less total norepinephrine by infusion and having a lower fluid balance.<sup>1</sup>

We congratulate the authors for having performed such innovative research on perioperative hemodynamic optimization to improve patient's postoperative outcome. Nonetheless, we have a few comments and questions.

1. In this study, the median [interquartile range] minimum "individualized" MAP target (within 10% of baseline) was significantly higher (81 [76 to 81] mmHg) than expected based on recommendations by the Perioperative Quality Initiative consensus on intraoperative blood pressure, risk, and outcomes for elective surgery (*i.e.*, MAP greater than 60 to 70 mmHg).<sup>2</sup> We suspect that the MAP measured during the preoperative screening, defined as "baseline" (90 [85 to 90] mmHg), might be an overestimate of the individual normal daytime MAP due to the "white coat" effect, known to affect up to 30% of subjects.<sup>3</sup> This point is even more important because general anesthesia represents a state of reduced sympathetic nervous system and metabolic activities during which the MAP threshold for adequate organ perfusion is likely reduced in comparison with daytime. A potential more physiologic approach was reported by Saugel *et al.*,<sup>4</sup> who suggest that automated ambulatory measurement of MAP during physiologic sleep is a more relevant target during general anesthesia. As a consequence of the high level of MAP triggering intervention in the current study, the reported reduction in the duration of intraoperative hypotension in the computer-assisted group (−21.1% [95% CI, −15.9 to −27.6%]) was potentially overestimated.
2. In their sample calculation, the authors estimated the control group to have a total duration of  $12 \pm 8\%$  of intraoperative case time with hypotension based on their previous data. However, the control group experienced hypotension at nearly twice the anticipated rate (21.5% [14.5 to 31.8]). If this is indeed well-established standard of care, it would be helpful to understand the authors' insight into potential causes of this significant discrepancy with their initial estimate.
3. Last and not least, in their rationale, the authors mentioned the finding by Walsh *et al.*<sup>5</sup> regarding the increase in risk associated with every 5 min spent under the MAP threshold of 55 mmHg. The current presentation of the results (cumulative duration of hypotension) does not distinguish between repetitive brief (*e.g.*, less than 1 to 2 min) episodes of hypotension *versus* prolonged episodes, which probably differ in risk for end organ damage and therefore clinical relevance. Would such an analysis (*i.e.*, filtering out very short durations of hypotension) modify the conclusions of the authors?

### Competing Interests

Dr. Cholley has received honoraria for participation on advisory boards and lecturing fees from Edwards

Lifesciences (Irvine, California), Orion Pharma (Espoo, Finland), Amomed (Wien, Austria), and Nordic Pharma (Paris, France). Dr. McCluskey has received honoraria from Edwards Lifesciences for advisory work and speaker's support. The other authors declare no competing interests.

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# Individualized Fluid and Vasopressor Therapy: Reply

## In Reply:

We thank Dr. Soussi *et al.*<sup>1</sup> for their very relevant comments regarding our recent article on computer-assisted individualized hemodynamic management.<sup>2</sup>

We agree that the reference mean arterial pressure (MAP) measured during the preoperative consultation might have overestimated their “normal” daytime MAP due to a potential “white coat” effect, and that this overestimation may have affected our conclusions. Although it would have been appealing to obtain an automated ambulatory MAP measurement during sleep the day before surgery using noninvasive finger cuff technology as recently proposed,<sup>3</sup> we unfortunately don’t have access to this device at our hospital (yet). It is also important to note that at least 40% of our studied population had chronic hypertension, and in a large randomized controlled trial conducted in chronic hypertensive patients, Wu *et al.*<sup>4</sup> demonstrated that maintaining a MAP between 80 and 95 mmHg decreased the incidence of acute kidney injury (AKI). Additionally, a separate guideline recommendation article also suggests that maintaining a MAP higher than the general threshold of 65 mmHg seems appropriate for preventing AKI in hypertensive patients.<sup>5</sup> As a result, we felt that maintaining a MAP at a minimum of 80 mmHg in our study can be justified, although future research always has the potential to adjust our current perioperative goals.

The discrepancy between the estimated and the observed total duration of intraoperative case time with hypotension in the control group can likely be explained by a lack of compliance on the part of clinicians in that group. Although the anesthesiologists intended to maintain a median MAP value of 80 mmHg, it is easy to understand that MAP values between 75 to 79 mmHg may not have necessarily elicited an immediate response. This phenomenon has already been well described by Sessler *et al.*<sup>6</sup> in their triple-low alerts study and recently by Maheshwari *et al.*<sup>7</sup> in the hypotension prediction index study. Both studies reported that most of the system alerts were not subsequently followed by an appropriate response in accordance with the predefined algorithm. It was also possible that sometimes clinicians may have simply ignored the alert. Therefore, we feel that despite an individualized hemodynamic management protocol designed to maintain MAP within 90% of baseline MAP, clinicians may have intermittently not reacted to MAP values just below that target levels.

Last, we agree with Soussi *et al.* that brief repetitive episodes of less than 1 to 2 min of hypotension *versus* prolonged episodes could differ in risk of end-organ damage, despite a similar cumulative duration of hypotension. However, our small study was not designed to answer this important question, and it should be investigated in the future with an appropriately powered and designed protocol.

## Competing Interests

Drs. Joosten and Rinehart are consultants for Edwards Lifesciences (Irvine, California) and have ownership interest in Perceptive Medical, Inc. (Newport Beach, California), which is developing closed-loop physiologic management systems. In addition, Dr. Rinehart has ownership interest in Sironis (Newport Beach, California), and Sironis has developed a fluid closed-loop system that has been licensed to Edwards Lifesciences and was used in this study as a decision support system (assisted fluid management). The closed-loop system for vasopressor administration used in this study is new and is the sole creation of two of the authors (Drs. Joosten and Rinehart). Dr. Van der Linden has received, within the past 5 yr, fees for lectures and consultancies from Fresenius Kabi GmbH (Bad Homburg, Germany), Aguetant Medical SA (Lyon, France), Nordic Pharma (Antwerpen, Belgium), and Vifor Pharma (Antwerpen, Belgium). The other authors declare no competing interests.

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## Anesthesia and Surgery in Space: Comment

To the Editor:

We read the recent article penned by Komorowski *et al.*<sup>1</sup> with great interest, and we congratulate the authors on a well-composed and thought-provoking article addressing space exploration and the challenges of medical care, especially anesthesia, in this austere environment.

Although undersea and hyperbaric medicine is often associated with treating conditions secondary to increases in ambient pressure, such as those arising from scuba diving, it also aids in understanding and treating the pathophysiology

of exposures to hypobaric conditions, like those experienced by pilots or astronauts.

In fact, entering any current space suit from a living environment, such as the International Space Station or a lunar lander, requires a decompression to a lower ambient pressure.<sup>2</sup> Human trials involving decompression from sea level (1 atmosphere absolute [ATA]) to ambient pressure of the U.S. space suit (0.3 ATA) has resulted in decompression sickness in up to 20% of exposures and venous gas emboli in up to 62%.<sup>3</sup> Furthermore, knee pain due to decompression sickness was experienced by Gemini X astronaut Michael Collins in 1966.<sup>4</sup>

Although such events in space have thus far been rare, increased numbers of human exposures and time in space will raise the probability of such an event. Thus, we believe training in undersea and hyperbaric medicine is crucial and preparatory for the future medical challenges inherent with interplanetary spaceflight. Currently, there are 10 Accreditation Council for Graduate Medical Education–approved training programs in undersea and hyperbaric medicine.<sup>5</sup>

### Competing Interests

Dr. Moon reports payment for contribution to the Merck Manual (Merck and Co., Inc., Kenilworth, New Jersey). Dr. Covington declares no competing interests.

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